

U.S.S.N. 09/715,965  
Filed: November 17, 2000  
Amendment

## APPENDIX: Clean Copy of Claims as Amended

*treat Cancer, etc.*

C1 1. (three times amended) A method to decrease angiogenesis comprising administering to a site in an individual in need of treatment thereof for an established disorder requiring angiogenesis an effective amount of a purified chondroitinase to decrease angiogenesis at the site, wherein the decrease in angiogenesis is measured as a decrease in endothelial cell proliferation or a decrease in the formation of capillary-like structures.

C2 2. (amended) The method of claim 1 wherein the enzyme is selected from the group consisting of chondroitinase AC from *Flavobacterium heparinum*, chondroitinase B from *Flavobacterium heparinum*, a chondroitin sulfate degrading enzyme from *Bacteroides* species, a chondroitin sulfate degrading enzyme from *Proteus vulgaris*, a chondroitin sulfate degrading enzyme from *Micrococcus*, a chondroitin sulfate degrading enzyme from *Vibrio* species, a chondroitin sulfate degrading enzyme from *Arthrobacter aurescens*, these enzymes expressed from recombinant nucleotide sequences in bacteria and combinations thereof.

3. The method of claim 1 wherein the enzyme is a mammalian enzyme.

C3 4. (amended) The method of claim 8 wherein the enzyme is a chondroitinase AC.

5. (amended) The method of claim 1 wherein the chondroitinase is chondroitinase

AC.

C4 6. (twice amended) The method of claim 1 wherein the enzyme is administered to an individual having cancer as evidenced by palpable tumors.

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7. The method of claim 6 wherein the cancer is a solid tumor and the enzyme is chondroitinase AC.

C5 8. (amended) The method of claim 1 wherein the individual has a disorder in which angiogenesis is involved, the disorder being selected from the group consisting of rheumatoid arthritis; psoriasis; ocular angiogenic disease, rubeosis; Osler-Webber Syndrome; myocardial angiogenesis; plaque neovascularization; telangiectasia; hemophiliac joints; angiofibroma; Crohn's disease, atherosclerosis, scleroderma, hypertrophic scarring, adhesions, cirrhosis of the liver, pulmonary fibrosis following acute respiratory distress syndrom or other pulmonary fibrosis of the newborn, endometriosis, polyposis, obesity, uterine fibroids, prostatic hypertrophy, and amyloidosis.

9. The method of claim 1 wherein the enzyme is administered systemically.

C6 10. (amended) The method of claim 1 wherein the enzyme is administered locally at or adjacent a site in need of treatment.

11. The method of claim 1 wherein the enzyme is administered in a controlled and/or sustained release formulation.

19. The method of claim 7 wherein the dosage is in the range of 0.1 to 250 IU chondroitinase AC/tumor for tumors in the size range from 20 mm<sup>3</sup> to 15 cm<sup>3</sup>.

20. The method of claim 1 wherein the enzyme is administered in combination with another active agent selected from the group consisting of antibiotics, cytokines, cytotoxic agents, and anti-inflammatories.

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21. The method of claim 7 wherein the enzyme is administered after excision of the tumor.

22. The method of claim 9 wherein the enzyme is administered by a route selected from the group consisting of intravenous, intra-cranial, and depo.

23. The method of claim 9 wherein the enzyme is administered using an infusion pump.

24. The method of claim 1 wherein the enzyme is chondroitinase B.

25. The method of claim 8 wherein the enzyme is chondroitinase B.

26. The method of claim 1 wherein the individual has a disorder in which angiogenesis is involved, the disorder being selected from the group consisting of disease of excessive or abnormal stimulation of endothelial cells, diseases that have angiogenesis as a pathologic consequence, and scarring following transplantation,

27. The method of claim 1 wherein the enzyme is administered topically.

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